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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte THOMAS T. HUBSCHER and
ERIK P. LILLEHOJ

Appeal No. 2001-2410
Application No. 08/914,700

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-21, all of the claims remaining. Claim 1 is representative and reads as follows:

1. A method for the quantitative or qualitative detection of an analyte in a liquid biological specimen comprising the steps of:

   (a) forming a test sample by adding to a biological specimen, (i) a binding substrate in a liquid phase selected from the group consisting of a ligand and an antiligand which specifically binds the analyte, and (ii) a detector substance in a liquid phase selected from the group consisting of a colloidal metal labeled ligand and a colloidal metal labeled antiligand, to form

a test sample containing a precipitable complex if the analyte is present and forming no such complex in the absence of the analyte in the biological specimen;

(b) applying the test sample to a defined zone on a porous support, the support having a maximum effective pore size smaller than a complex formed between the analyte, the binding substance and the detector substance and having minimal effective pore size larger than each of the analyte, the binding substance and the detector substance if a precipitable complex with an analyte is not formed, so that the analyte, the binding substance and the detector all can pass through the support, no solid phase particles or insoluble components being introduced into the defined zone on the porous support; and

(c) assessing the defined zone for color development caused by the formation of the complex formed by the analyte, the binding substance and the detector substance, the color development correlating with the presence of the analyte in the test sample.

The examiner relies on the following references:

Leuvering	4,313,734	Feb. 02, 1982
Hossom et al. (Hossom)	4,623,461	Nov. 18, 1986
Olsen et al. (Olsen)	4,853,335	Aug. 01, 1989
Akers, Jr.	5,565,366	Oct. 15, 1996

Claims 1-4 and 6-15 stand rejected under 35 U.S.C. § 103 as obvious in view of Hossom and Leuvering.

Claim 5 stands rejected under 35 U.S.C. § 103 as obvious in view of Hossom, Leuvering, and Olsen.

Claims 16-18, 20, and 21 stand rejected under 35 U.S.C. § 103 as obvious in view of Hossom, Leuvering, and Akers.

Claim 19 stands rejected under 35 U.S.C. § 103 as obvious in view of Hossom, Leuvering, Olsen, and Akers.

We reverse.

Background

The specification discloses a method for detecting analytes using "non-captive substrate liquid phase immunoassay techniques." See page 2. The specification states that

> [o]bservations of colloidal gold or silver concentrations have been used in immunoassays in conjunction with solid phase diffusion assays. For example, European Patent No. 207,152 discloses a solid phase diffusion assay utilizing a porous sheet having ligands or receptors prebound to the sheet prior to the application of an analyte and a colloidal gold or silver labeled ligand or receptor.

Id. This method, however, has the drawback that the "ligand or antiligand coated porous films must be specifically tailored for a particular analyte and . . . may be ineffective if the affinity of the substrate bound antiligand for the labeled analyte is low." Id.

The specification also discusses a sandwich immunoassay method that involves "premixing a biological specimen with: (1) a colloidal gold labeled ligand or antiligand and (2) solid phase captive particles coated with a ligand or antiligand and applying the subsequent mixture onto the surface of a porous film." Id. This method also has a drawback, in that the solid phase captive particles (e.g., latex particles) "may distort the visual detection measurements because uncoupled captive particles may block the pores of the substrate and prevent rapid passage of uncoupled colloidal gold." Id., pages 2-3.

The specification discloses an alternative immunoassay method in which a liquid biological specimen is mixed with

> (a) a binding substance of a ligand, antiligand or receptor capable of binding the analyte and (b) a detector substance of a colloidal metal labeled ligand or antiligand. . . . The test sample is then applied onto a defined zone of an insoluble porous support film having a pore size impassable to a complex formed between the analyte, if present, with the binding substance and the detector substance, but passable to the binding substance and detector substance while remaining uncomplexed in the absence of the desired analyte.

Id., pages 3-4 (emphasis added). Thus, "[if] the analyte is present in the test specimen, the analyte binds with both the detector substance and the binding substance to form a visually discernable precipitable complex on the surface of the porous support film." Id., page 4.

Discussion

The claims are directed to a method and kit for carrying out the disclosed immunoassay method. Thus, for example, claim 1 is directed to a method comprising forming a test sample by mixing a biological specimen with "a binding substrate [sic, substance] . . . which specifically binds the analyte" and a colloidal metal-labeled detector substance; the binding substance and the detector substance both bind to the analyte. The test sample is then applied "to a defined zone on a porous support, the support having a maximum effective pore size smaller than a complex formed between the analyte, the binding substance and the detector substance and having a minimal effective pore size larger than each of the analyte, the binding substance and the detector substance if a precipitable complex with an analyte is not formed, so that the analyte, the binding substance

and the detector substance all can pass through the support." Finally, the support is assessed for color development, the presence of color in the defined zone being indicative of the presence of the analyte in the test sample.

The examiner rejected all of the claims as obvious over the prior art. All of the examiner's rejections rely on the combination of Hossom and Leuvering. The examiner concluded that these references would have rendered obvious the basic method of claim 1. The examiner characterized Hossom as disclosing all of the limitations of the claimed method except for the use of colloidal metal as the label. See the Examiner's Answer, pages 3-4. She relied on Leuvering to meet this limitation, and concluded that "[it] would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the enzyme labels of Hossom et al[.] with the metal sol particles of Leuvering because Leuvering teaches that the use of metal sol particles provides the additional advantage of a more sensitive assay than the known radio or enzyme immunoassays." Id., page 5.

The examiner acknowledged that "Hossom et al[.] do not specifically state that the filter membrane of their invention has pore sizes that will allow the passage of any non-complexed reagents." Id. She concluded, however, that this limitation was inherently present in Hossom's disclosure. See id.:

> [A] skilled artisan can clearly see that the pore sizes of the instant invention (0.2 – 12 microns, page 8) are the same with the pore sizes of the membrane of Hossom et al[.], therefore, it is expected that the filter of Hossom et al[.] will have the same inherent function as that of the instant invention, i.e.[,] allowing the passage of the analyte, the binding substance and the detector substance if a precipitable complex with an analyte is not formed. And because

> Hossom et al[.] teach that the result of the assay can be read directly on the filter membrane, it clearly indicates that any complexes formed between the labeled reagent, the binding substance and the analyte are retained on the filter membrane.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). The obviousness analysis must be based on the invention as a whole. See General Foods Corp. v. Studiengesellschaft Kohle mbH, 972 F.2d 1272, 1275, 23 USPQ2d 1839, 1840 (Fed. Cir. 1992) ("[E]ach claim is an entity which must be considered as a whole." (emphasis in original)).

"The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art." In re Young, 927 F.2d 588, 591, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991). That is, the test is "whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention." In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

In this case, we conclude that the examiner has not made out a prima facie case of obviousness. The claims on appeal place specific limitations on the porous support used in the claimed method. The porous support must have "a maximum effective pore size smaller than a complex formed between the analyte, the binding substance, and the detector substance and . . . [a] minimal effective pore size larger than each of the analyte, the binding substance and the detector substance if a precipitable complex with an analyte is not formed, so

that the analyte, the binding substance and the detector substance all can pass through the support."

Hossom does not disclose a porous support meeting these limitations. Rather, Hossom discloses a device that is "suitable for use with any of the conventional procedures used for analyte assays." Column 2, lines 31-33. Hossom provides the following guidance with regard to filters:

> In the preferred embodiment the filter means is made of a porous material capable of drawing liquid within its structure by capillary action. The pores of the filter should be sufficiently small to effect a filter separation of an insolubilized component within the liquid from a solubilized component. . . . It has been found that a filter means, which comprises a microporous membrane having substantially uniform pores between 25 nanometers and 25 micrometers, has the characteristics described and is useful in performing immunoassay testing procedures for which this device is particularly useful.

Column 4, lines 38-58 (reference numerals omitted).

Hossom also discloses that the device

> may also be used for specific immunochemical assays by "prespotting" the reaction zone with an analyte specific reactant. . . . For example, the manufacturer of the device could place in the filter reaction zone a binding protein to which an antibody is bound, which antibody is immunologically reactive with a specific antigen. Thus, a specimen being tested for the specific antigen would be . . . [applied] onto the upper surface of the reaction zone of [the] filter. The solution would be wicked through the reaction zone which has been prespotted . . . If the specific antigen is present in the specimen, it binds to the antigen's specific antibody which itself is already immobilized within the filter and would remain in the reaction zone after the washing step. The unbound antigen and other material within the solution are effectively washed away from the reaction zone and into the absorbent means. Finally, an antibody labeled with a detectable enzyme . . . is poured through the test device and binds to the bound antigen.

Column 5, lines 25-60 (reference numerals omitted).

These disclosures bear some resemblance to the instantly claimed method, in that they concern immunological detection using a filter to immobilize the analyte of interest. However, Hossom does not suggest with any specificity the limitations of the method claimed by Appellants. Hossom does not teach, for example, a method that involves mixing a test sample with a liquid-phase binding substance and a liquid-phase labeled detector substance, nor does Hossom suggest with any specificity a porous support meeting the limitations of instant claim 1.

We do not agree with the examiner that the pore size limitation of the instant claims is met inherently by Hossom. When the examiner relies on a theory of inherency, the material alleged to be inherently disclosed must necessarily be present. See In re Robertson, 169 F.3d 743, 49 USPQ2d 1949 (Fed. Cir. 1999). See also In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981): "'Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. [Citations omitted.] If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.'" (quoting Hansgirg v. Kemmer, 102 F.2d 212, 214, 40 USPQ 665, 667 (CCPA 1939) (emphasis and bracketed material in original)).

The examiner has pointed to no evidence showing that operation of Hossom's device would necessarily involve using a porous support meeting the

pore size limitation recited in the instant claims. The examiner therefore has not met her burden of showing that Hossom inherently meets that limitation of the claims.

Nor has the examiner pointed to any disclosure in the secondary references that would have suggested the pore size limitation in the claims. The examiner relied on Leuvering and the other secondary references only to meet the limitation requiring a colloidal gold-labeled detector substance (Leuvering) and certain limitations of the dependent claims (Olsen and Akers). These references therefore do not make up for the deficiencies of Hossom. The rejections under 35 U.S.C. § 103 are reversed.

Other Issues

Some of the claims on appeal (specifically, claims 17-21) are directed to a kit rather than a method. The examiner rejected the kit claims together with method claim 16 as obvious in view Hossom, Leuvering, and Akers. The rationale of the rejection was the same as discussed above, with Akers cited as "teach[ing] an assay to detect antigens such as . . . C-reactive proteins." Examiner's Answer, page 6. Akers was also cited as "teach[ing] assembling all of the necessary reagents for the assay into kits." Id.

We have concluded that Hossom and Leuvering do not disclose or suggest all of the limitations of the claimed method, especially the specifically recited porous support. This conclusion requires reversing the examiner's rejection of the kit claims as well as the method claims.

However, we note that most of the kit claims are not limited to kits for detecting C-reactive protein, and would appear to read on any kit comprising the recited porous support, binding substance, and detector substance, for detecting any desired analyte. Upon return of this application, the examiner should consider whether the rejections of record adequately address the patentability of the kit claims. Olsen appears to be especially relevant, although we have not thoroughly reviewed the reference's disclosure with respect to the claimed kits, and we take no position on whether the reference renders the kit claims unpatentable. The examiner is in a better position to make that decision.

In considering the patentability of the kit claims, the examiner should bear in mind that prima facie obviousness does not require the prior art references to suggest combining their disclosures for the same reason that Appellants combined them. See In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) ("[I]t is not necessary in order to establish a prima facie case of obviousness that . . . there be a suggestion in or expectation from the prior art that the claimed compound or composition will have the same or a similar utility as one newly discovered by applicant." (emphases in original)).

Summary

The references relied on by the examiner do not support a prima facie case under 35 U.S.C. § 103. The rejections for obviousness are therefore reversed.

REVERSED

WILLIAM F. SMITH Administrative Patent Judge	)
	) BOARD OF PATENT
TONI R. SCHEINER Administrative Patent Judge	) APPEALS AND
	) INTERFERENCES
ERIC GRIMES Administrative Patent Judge	)

Aaron B. Retzer
Epstein Edell and Retzer
Suite 400
1901 Research Boulevard
Rockville, MD 20850-3167

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